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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,916	07/09/2001	Hiroshi Shiku	P20854	1184

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,916	SHIKU ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 5/20/05 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment, remarks, and IDS, filed 5/20/05, have been entered.

2. Claims 1-20, and newly added Claims 21-26, are being acted upon.

3. Applicant's summary of the interview of 4/18/05 is noted.

4. In view of Applicant's remarks, the previous rejections of Claims 13 and 14 under 35 U.S.C. 103(a) over Nestle et al. (1998, IDS) in view of Jiang et al. (1995, of record) has been withdrawn. In particular, it is noted that the mannan of Nestle et al. is not hydrophobized.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

6. Claims 1-3, 6, 11, 12, 15, 18, and 20 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kohno et al. 1996.

As set forth previously, Kohno et al. teaches a DC APC capable of inducing cellular immunity, said cell having been produced by reacting *in vitro* with the hydrophobized polysaccharide pullulan (see particularly page 213, column 1).

Applicant's arguments, filed 5/20/05, have been fully considered but they are not persuasive. Applicant argues that the complex of Claim 1 is actually a conjugate or an aggregate of hydrophobized polysaccharide and antigen and APC and that the reference does not teach said complex.

Neither in the specification nor claims disclose a conjugate nor aggregate as asserted by Applicant. The "complex" of the claims is not further defined. Applicant cannot now redefine the invention of the claims. The reference teaches a complex of hydrophobized polysaccharide and antigen placed *in vitro* with, and thus, "reacted" with, an APC, thus, preparing the cell capable of inducing cellular immunity set forth in the claims. Note that a "hydrophobized" polysaccharide is disclosed as being a polysaccharide with additional alkyl groups attached. Alkyl groups comprise any H_2-C-R, which would include any protein antigen.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-20, and newly added Claims 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nestle et al. (1998, IDS) in view of Gu et al. (1997, IDS).

As set forth previously, Nestle et al. teaches a method for inducing cellular immunity comprising isolating a DC APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration (see particularly Methods, page 331, column 2 - page 332, column 1).

The reference differs from the claimed invention only in that it does not teach an APC loaded with the ErbB-2 antigen by reacting with a complex comprising a hydrophobized polysaccharide comprising mannan or a polysaccharide comprising the limitations of Claim 4 wherein the sterol is cholesterol.

Gu et al. teaches that a cholesterol bearing mannan polysaccharide complexed to an ErbB-2 antigen (an antigen overexpressed in a wide range of human adenocarcinomas, see Abstract) can be used to induce CD8+ CTLs (page 19, column 2, second full paragraph and page 23, column 1) by a mechanism of facilitating the entry of the antigen into the MHC Class I pathway for presentation by APCs (see particularly page 24, column 1, first full paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a product for, and perform a method for, inducing cellular immunity comprising isolating a DC APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration, as taught by Nestle et al. One of ordinary skill in the art at the time of the invention would have been motivated to employ the cholesterol bearing mannan polysaccharide complexed to an ErbB-2 antigen of Gu et al. given the teachings of the reference that the ErbB-2 antigen is overexpressed in a wide range of human adenocarcinomas (and would thus provide an obvious target for immunotherapy) and that

the use of the cholesterol bearing mannan polysaccharide facilitates the entry of the antigen into the MHC Class I pathway for presentation by APCs.

Applicant's arguments, filed 5/20/05, have been fully considered but they are not persuasive. Applicant briefly summarizes the teachings of Gu et al., in particular, Applicant indicates that the reference teaches a hydrophobized polysaccharide-antigen complex. Applicant asserts that the claimed invention has advantages over the invention of the combined teachings of Gu et al. and Nestle et al., "In particular, Applicants' invention comprises the inclusion of an antigen-presenting cell with a complex comprising a hydrophobized polysaccharide and antigen."

Applicant is advised that the invention of the combined references is "an antigen-presenting cell with a complex comprising a hydrophobized polysaccharide and antigen".

Applicant appears to then assert a superior/unexpected result and compares Figure 1 of Wang et al. *Int. J. Oncol.* (1999) with Figure 5 of Gu et al. and Figure 5 of Wang et al.

Applicant is advised that it is well-established that it is inappropriate to assert superior or unexpected results not disclosed in the specification in an attempt to overcome an art rejection. Additionally, it is unclear how or why Applicant can or would compare Figure 1 of Wang et al. *Int. J. Oncol.* (1999), which discloses *in vivo* tumor size after DC vaccination as a function of time, with Figure 5 of Gu et al., which discloses *in vitro* spleen cell killing activity, with Figure 5 of Wang et al., which discloses another example of *in vivo* tumor size after DC vaccination as a function of time.

Applicant argues that neither of the references teaches the invention of the instant claims.

Clearly, if either of the references alone taught the invention of the claims the rejection would have been made under 35 U.S.C. 102 and not 35 U.S.C. 103(a). As set forth in the rejection above, proper motivation has been provided to use the hydrophobized antigen complex of Gu et al. in the method of inducing cellular immunity of Nestle et al., i.e., to achieve superior antigen presentation and T cell activation given the demonstrated ability of the hydrophobized polysaccharide-antigen complex of Gu et al. to facilitate antigen entry into

the MHC Class I pathway. Finally note that the Examiner's burden is merely to establish motivation to produce the claimed invention. Said motivation need not be Applicant's. Said motivation has been properly established as set forth above.

9. The following are new grounds for rejection.

10. Claims 1-20, and newly added Claims 21-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nestle et al. (1998, IDS) in view of Gu et al. (1998, of record).

Nestle et al. has been discussed above.

The reference differs from the claimed invention only in that it does not teach an APC loaded with antigen (ErbB2 also known as HER2) by reacting with a complex comprising a hydrophobized polysaccharide comprising mannan or pullulan, or a polysaccharide comprising the limitations of Claim 4 wherein the sterol is cholesterol.

Gu et al. teaches that a cholesterol bearing mannan or pullulan polysaccharide complexed to a HER2 antigen (see Materials and Methods) can be used to induce CD8+ cellular immunity (see particularly Figures 1 and 4), while antigen alone is ineffective, by a mechanism of facilitating the entry of the antigen into an APC through a carbohydrate-recognizing receptor such as DEC-205, and entry into the cytosol (for transport to MHC Class I) after phagocytosis (see particularly page 3389, column 2-3390).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a product for, and perform a method for, inducing cellular immunity comprising isolating a DC APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration, as taught by Nestle et al. One of ordinary skill in the art at the time of the invention would have been motivated to employ the cholesterol bearing mannan or pullulan polysaccharide complexed to a HER2 antigen of Gu et al. given the teachings of the reference that hydrophobized polysaccharide-antigen complex facilitates the entry of the antigen into an APC through a carbohydrate-recognizing receptor such as DEC-205, and entry into the cytosol (for transport to MHC Class I) after phagocytosis, for superior antigen presentation and cellular immunity.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-26 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) a complex formed from interaction of a hydrophobized polysaccharide and an antigen (Claim 1 or 11).

Applicant fails to indicate where support for the term "interaction" in the product and method of the instant claims is found in the specification.

No support has been found.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

15. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

8/4/05

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